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14. ABSTRACT

This is a two-year randomized trial of the effects of oral contraceptives on bone mass and stress fracture incidence among 151 female competitive distance runners in the age range 18-25 years. The Coordinating Center is at Stanford University and bone mass is being measured at five sites: Massachusetts General Hospital, University of California Los Angeles, University of Michigan, Stanford University/Palo Alto VA Medical Center, and Helen Hayes Hospital in West Haverstraw NY. Athletes were recruited mostly from the areas around these five clinical sites. Over the five clinical sites, 151 runners were randomized, and follow-up continues. Follow-up will be completed in 2005, and final results of the study should be available in 2006.

15. SUBJECT TERMS

bone mass, oral contraceptives, physical activity, randomized trial, epidemiology, stress fracture, osteoporosis

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(5) INTRODUCTION

Highly trained female athletes may experience loss of menses because of their participation in intense physical activity. Previous cross-sectional research has shown that women with exercise-induced menstrual irregularities have a significantly higher frequency of stress fractures and low bone mass than normally menstruating controls. Longitudinal studies suggest that these women are losing bone mass over time. Low serum estrogen levels are believed to be a principal cause of the bone loss. If so, re-establishing normal estrogen levels in these women should prevent or retard bone loss and decrease the incidence of stress fracture. This study is a two-year randomized trial of the effect of oral contraceptives on bone mass and stress fracture incidence among 151 female cross country runners in the age range 18-25 years. The Coordinating Center is at Stanford University and bone mass is being measured at five sites: the Massachusetts General Hospital, the University of California Los Angeles, the University of Michigan, Stanford University/Palo Alto VA Medical Center, and the Helen Hayes Hospital in West Haverstraw, NY. Athletes are being recruited mostly from the areas around these five clinical sites.

(6) BODY

Below we summarize (a) our progress through year 7, and (b) our plans for completing the study.

(a) Progress through year 7:

As of the time of this writing (October 1, 2005), of the 151 runners randomized, 118 have completed the study, of whom 99 had two follow-up visits and 19 only one follow-up visit. An additional 5 have had one follow-up visit and are on time to have a second follow-up visit and one very delinquent participant is about to have one follow-up visit before the end of the month. Another 2 have had one follow-up visit, but are delinquent for their second follow-up visit.

Thus, at this time we expect to have at least some follow-up bone mineral density measurements on 126 (83.4%) of the 151 who were randomized. Of the remainder, 19 have either withdrawn or are lost to follow-up, and 6 may be lost, although we have not quite given up. During year 7 specifically, 23 have completed the study to date. We hope that the additional 6 participants will have their final bone mineral density measurement before data collection ends, especially if we extend data collection to the first 1-2 weeks of November.

(b) Plans for completing the study: We expect to complete data collection by November 2005, and to have data analysis for the primary objectives completed in 2006.

(7) KEY RESEARCH ACCOMPLISHMENTS: During the past budget year we have concentrated on data collection rather than publications. However, below under Conclusions we report on some interesting interim results

(8) REPORTABLE OUTCOMES: None during the past year.

(9) CONCLUSIONS: We will have no firm conclusions to report on the primary hypothesis of the study until the end of the trial. However, an interim data analysis was conducted in July 2005. At that time, at least one follow-up DXA measurement was available for 123 women. We are not repeating findings on stress fracture occurrence that were reported in the year 6 progress report

Participants gained small, but significant, amounts of whole body bone mineral content (BMC) and skeletal area during the study, suggesting that the skeleton continues to grow a small amount into the third decade of life. The largest skeletal gains were seen in the women who were

amenorrheic (21.4g BMC/year) or oligomenorrheic (18.0g BMC/year) at baseline, compared with those who were eumenorrheic (6.0g BMC/year).

Using an intention-to-treat analysis, there was no evidence that being randomized to oral contraceptives (OCs) was associated with larger gains in whole body BMC or in hip or spine bone mineral density (BMD) for any menstrual group. Among eumenorrheic women, the mean annual change in spine and hip BMD was close to zero in both the treatment and control groups. Oligomenorrheic and amenorrheic women had small increases in spine BMD (0.0058 g/cm^2/year and 0.0178 g/cm^2/year, respectively) that correlated strongly with increasing period regularity, but not with randomization to treatment. Amenorrheic women in both randomization groups additionally had small increases in hip BMD (0.0054 g/cm^2/year).

We also conducted a non-intention-to-treat analysis among the women who were amenorrheic or oligomenorrheic at baseline (62% regained normal menses by the end of the study). Women who spontaneously regained periods and those who regained their periods through the use of OCs had larger gains in whole body BMC and spine BMD compared with those who remained irregular. Women who used OCs gained bone faster initially, but women who spontaneously resumed periods had larger gains in BMC and BMD after two years (average yearly change in BMC: spontaneous resumption: 40.0 g/year; OCs: 19.1 g/year; remained irregular: 0.1g/year; average yearly change in spine BMD: spontaneous resumption: 0.013 g/cm^2/year; OCs: 0.008 g/cm^2/year; remained irregular: 0.003 g/cm^2/year).

(10) REFERENCES: None

(11) APPENDICES: None.